NAVAL HEALTH RESEARCH CENTER

REPRODUCTIVE OUTCOMES AMONG FEMALE GULF WAR ERA U.S. MILITARY VETERANS: NO EVIDENCE OF INCREASED MORBIDITY

P. A. Sato
K. M. Hiliopoulos
L. Wang
C. M. Anderson
D. R. Kamens
J. M. Major
C. B. Morn
P. P. Poblete
A. C. Zau
G. C. Gray

20040121 040

Report No. 00-38

Approved for public release; distribution unlimited.

NAVAL HEALTH RESEARCH CENTER P. O. BOX 85122 SAN DIEGO, CA 92186-5122



BUREAU OF MEDICINE AND SURGERY (MED-02) 2300 E ST. NW WASHINGTON, DC 20372-5300



Reproductive Outcomes among Female Gulf War Era US Military Veterans:

No Evidence of Increased Morbidity

Paul A. Sato, M.D., MPH¹
Katia M. Hiliopoulos, MPH, MBA^{1,2}
Linda Wang, BS¹
Christy M. Anderson, BS^{1,3}
Deborah R. Kamens, MBA¹
Jacqueline M. Major, MS^{1,3}
Cassandra B. Morn, BA¹
Pamela P. Poblete, MPH^{1,4}
Andrew C. Zau, MPH¹
Gregory C. Gray, M.D.¹

¹DOD Center for Deployment Health Research Naval Health Research Center P. O/ Box 85122 San Diego, California 92186-5122

²Agouron Pharmaceuticals, Inc., San Diego

³Tobacco Control Policies Project University of California, San Diego

⁴Center for Behavioral and Community Health Studies San Diego State university

26 October 2000

Report No. 00-38, supported by the Office of the Assistant Secretary of Defense, Health Affairs under research work unit DOD (HA) Reimbursable, Deployment Health Research Studies-60002. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the U.S. Government. Approved for public release; distribution unlimited. This research has been conducted in compliance with all applicable Federal Regulations governing the protection of human subjects in research.

ABSTRACT (244 words)

Context Veterans of the 1991 Gulf War may have had exposures that adversely affected their reproductive health. We examined the reproductive health of female Gulf War veterans in a nationally representative sample of 1991-era US military personnel.

Objective To compare the reproductive health, including subfertility, in a nationally representative, probability-based, sample of 1991-era female US military veterans, Gulf War deployed and non-Gulf War deployed.

Design Self-completed postal survey of outcomes in 1991-95, in a probability-based sample of 1991-era female veterans, with oversampling of the Gulf War deployed.

Setting Female US military veterans married and aged 18-33 years in 1991.

Study Participants A total 8251 subjects were randomly selected from the study domains, Gulf War deployed and nondeployed, after stratifying for branch of service and component.

Main Outcome Measures Self-reported reproductive outcomes, and subfertility.

Results In total, 2349 Gulf War and 2507 nondeployed veterans returned questionnaires, a participation rate of 71.7% after adjusting for 1477 undeliverable questionnaires. Gulf War veterans had a lower odds of total births (adjusted odds ratio (OR)=0.58, 95% confidence interval (CI) 0.44, 0.77), but experienced no increase in reproductive losses (adjusted OR=1.17, 95% CI 0.94, 1.45), subfertility (adjusted OR 1.11, 95% CI 0.85, 1.45), or in low birthweight births (adjusted OR 0.87, 95% CI 0.71, 1.07).

Conclusions Although female Gulf War veterans reported lower odds of births postwar, this did not appear to be associated with increased odds of subfertility, reproductive losses, or low birthweight birth outcomes.

A number of veterans of the 1991 Gulf War have complained of diverse symptoms and illnesses, possibly related to their military service in the Gulf. Children with birth defects have been born to Gulf War Veterans ¹, and concern has been voiced that these veterans may have had exposures that adversely affected their reproductive health ², ³. Suggestions have been made that, in addition to birth defects, these veterans may have an increased risk of infertility, miscarriages, and genitourinary tract problems ⁴.

Several studies have investigated the issue ⁵⁻⁹. Our study sought to respond to the need identified ¹⁰, ¹¹ for additional studies more representative nationally, and including all services (Army, Navy, Air Force, and Marine Corps) and components (active duty, reserve, and National Guard). Thus, the objective of our study was to examine the reproductive health of Gulf War veterans in nationally representative samples of 1991-era veterans including all services and components of the US military.

We report here on results among female US military veterans of the Gulf War era. In a companion article (Sato et al, Naval Health Research Center, unpublished manuscript), we report on the reproductive outcomes reported by male US military veterans studied through similar methods.

METHODS

Study population

Administrative, deployment, and demographic data for military personnel were obtained from the Defense Manpower Data Center (DMDC), Seaside, California. Female military veterans aged 18-33 years and married on February 1, 1991, who were in the Gulf War theater of operations between August 1, 1990, and July 31, 1991, were considered Gulf War veterans. Equivalent active duty, reserve, or National Guard military service members of the same era but

not deployed to the Gulf War theater of operations were defined as nondeployed veterans.

Deployment status was determined by DMDC from hostile fire pay records, and military unit deployment data.

This study was conducted in accordance with Protection of Human Subjects guidelines from the US Department of the Navy. The study protocol and informed consent issues were reviewed for this purpose by our institutional review board, and approval for the study obtained. Sample size

A sample size requirement of 8000 was determined based on detecting a 10 percent difference in rates of miscarriages between Gulf War veterans and nondeployed veterans. However, because we were dealing with a highly mobile and young population several years after the Gulf War, we selected a total of 10 000 individuals through a probability-based selection process, to make allowances for losses. The upper limit of acceptable β error was set at 0.20, and α error at 0.05. The estimated population rate for miscarriages of 10 percent was based on published rates, which ranged between 7 and 25 percent 12-14.

Of the approximately 377 000 female active-duty, reserve, and National Guard service members in 1991, approximately 50 000 were deployed to the Gulf War theater of operations. From this population, a stratified random sample of 5000, with proportionate allocation of the services and their components, was generated for each of the Gulf War and nondeployed veterans groups, for a total sample of 10 000. Where both spouses were military service members, the deployment status of the female spouse was determinant, and their responses were included here, in the analysis for female veterans.

Questionnaire

A four-page, self-completed postal questionnaire composed of both multiple-choice and open-ended questions was developed and field-tested. To enhance the validity and generalizability of the results, previously standardized questions were used in the questionnaire wherever possible. Sources of the questions included the Chicago Reproductive Health Survey (National Institute of Environmental Health Sciences, Research Triangle Park, NC, 1991), the National Survey on Family Growth, Cycle IV (National Center for Health Statistics, Hyattsville, MD, 1988), and the National Maternal and Infant Survey (National Center for Health Statistics, Hyattsville, MD, 1988). The questionnaire obtained demographic data (race/ethnicity and educational attainment), as well as information on military component, deployment, and information on the main outcomes measures: reproductive outcomes (livebirths, ectopic pregnancies, miscarriages/spontaneous abortions, and stillbirths), and subfertility (prolonged time to conception).

Pilot study

The survey questionnaires were pilot-tested among 14 individuals from outside the study population. Information from the pilot study was used to finalize the survey instrument.

Reproductive outcomes

For each reproductive outcome, respondents were encouraged to consult with their spouses and specify the date of the outcome, and whether the pregnancy had resulted in ectopic pregnancy (fetal death after extra uterine implantation), miscarriage (fetal death before 22 weeks of gestation), stillbirth (fetal death at or after 22 weeks of gestation), or livebirth (child born alive).

Information on birth weight, gestational age, and the sex of the infant was sought for each live birth. Subjects were asked to complete separate entries for each outcome in a multiple-birth pregnancy.

Subfertility

Subfertility was defined as last conception reported to have occurred after >12 menstrual cycles following cessation of contraceptive measures, and initiation of attempts at conception.

Data collection

Survey mailing process. The 10 000 initially selected subjects were mailed a preliminary study notification letter. These letters, mailed in February 1996, introduced the study to prospective participants and attempted to answer all anticipated questions about the study's purpose and objectives. It also sought to address any concerns about confidentiality of information that would be collected.

Study questionnaires were mailed to the 8251 subjects whose preliminary letters were not returned as undeliverable. Three rounds of questionnaires were mailed out over the next 18 months. Each mailing targeted those individuals who had not responded within 6 months to the preceding mailing. Specific study letterheads and logos were used for all correspondence with study subjects during the mailings to make our mailings easily distinguishable from other mail. To encourage responses, reminder postcards were sent 3 weeks after each mailing.

For subjects remaining on active duty, we routed surveys through their commanding officers. For the attention of these commanders, we attached letters from each service's Surgeon General, stressing the importance of this study and requesting that the commanding officers encourage potential study subjects to participate.

For subjects no longer on active duty, cover letters that incorporated comments describing other respondents' feelings about the significance and value of the study were included with the questionnaires, again to encourage participation.

Tracing correct addresses. Addresses obtained from the DMDC were used for initial mailings. If questionnaires were returned as undeliverable, additional sources were accessed to identify the most likely current valid addresses: the locator services of each branch of the military, Internal Revenue Service address data, and a commercial locator agency.

Collecting missing information. After completion of the third and final mailing, 633 subjects were re-contacted by telephone to obtain missing information on incomplete questionnaires, or to clarify responses. Five attempts to establish telephone contact were made to each apparently accurate phone number either obtained from the survey or acquired through an outside locator service. Attempts to contact by phone were made both during the week (2-3 times in the evening), as well as during weekends between 9 a.m. and 5 p.m. in the call recipients' time zone, before a subject survey was classified as "unreachable."

Supplemental information was obtained for 66 percent (418/633) with missing information. Information could not be obtained from the remaining 215. Of these, 65 had refused to provide further information over the telephone, or they could not be interviewed despite repeated attempts at contact through an apparently correct telephone number. Correct telephone numbers could not be identified for 150 others, despite multiple attempts.

Validation

To validate the answers provided by self-reported questionnaire, electronic hospital discharge records from US Department of Defense hospitals were compared with survey responses. Only subjects who remained on active duty during 1991-1995 were examined, since

only data on hospitalizations among service members on active duty were available. Responses were considered validated if the same or similar diagnosis was noted in the records within the same calendar year. No electronic data were available for hospitalizations outside Department of Defense facilities, or for ambulatory visits for the time period of interest, 1991-1995.

Statistical analysis

Analysis of reproductive outcomes. Frequencies of demographic data were generated for univariate analysis. Age was determined as of February 1, 1991. A multivariate logistic regression model was developed to generate odds ratios (OR), adjusted by age, race/ethnicity, highest level of education attained, military component, and pre-1991 reproductive outcomes. All reproductive outcomes occurring up to December 31, 1995, in the sample populations were included in the analysis. Post–Gulf War reproductive outcomes were defined as those occurring after May 31, 1991; outcomes at or before that date were defined as "pre-1991 outcomes". Univariate analysis was carried out for outcomes such as multiple births, ectopic pregnancies, and stillbirths, where sample size limitations excluded the use of multivariate models. Singleton and multiple births were analyzed separately.

Subfertility analysis. A separate logistic regression model was created to study subfertility as a potential adverse reproductive effect of Gulf War service. A multivariable model for subfertility, and adjusted for age, race/ethnicity, highest level of education attained, and military component was used to estimate adjusted OR. All previous reproductive outcomes were included as a covariate in the subfertility model.

RESULTS

The sample included 8251 selected subjects. Overall, 4856 (58.9%) of subjects returned a questionnaire. Of these, 421 were returned blank. Excluding the 1477 questionnaires that could not be delivered despite several attempts, participation was 71.7 percent (4856/6774).

Subjects whose highest level of education was high school graduation, who were Army veterans, and black were less likely to participate in the study (Table 1).

Total births

A total of 5209 singleton livebirths, and 88 twin/higher-order multiple births were reported by Gulf War veterans and nondeployed veterans. Of these, 2713 singleton births and 36 twin births occurred after the Gulf War. The distribution of these births was similar to that reported by the National Center for Health Statistics for the US in 1995 (Figure 1). Gulf War veterans had a fewer births in the 4 years following the conflict than nondeployed veterans (adjusted OR= 0.58, 95 percent confidence interval (CI) 0.44, 0.77), Table 2.

Macrosomia (birth weight ≥4000 g)

A total of 595 singleton macrosomic infants were reported, of which 323 occurred after the Gulf War. This represented 11.9 percent (323/2713) of all births post-Gulf War. No statistical association was found between Gulf War deployment and delivery of macrosomic babies following the Gulf War (adjusted OR= 0.86, 95 percent CI 0.66, 1.12) (Table 2).

Normal weight singleton births

There were 2238 normal weight singleton births post-Gulf War, representing 82.5 percent (2238/2713) of all singleton births following the Gulf War. A total of 4284 singleton babies born with normal birth weights (2500-3999 g) were reported by subjects. The odds of delivering

a normal birth weight infant did not differ significantly between Gulf War veterans and nondeployed veterans (adjusted OR= 0.87, 95 percent CI 0.71, 1.07) (Table 2).

Low birth weight (LBW) singleton births

Respondents reported 133 births with birth weights between 1500 and 2500 g, or 4.90 percent (133/2713) of all singleton births post-Gulf War. An addition, 19 (0.70 percent of births) were infants born with birth weights of <1500 g. Because of the small number of very low birth weight (<1500 g) births reported, all LBW births (<2500 g) were analyzed together. A total of 330 singleton LBW births were reported by subjects. No statistically significant association between Gulf War deployment and delivery of LBW infants post-Gulf War was identified (adjusted OR= 0.93, 95 percent CI 0.63, 1.38) (Table 2).

Twin and other multiple births

Respondents reported a total of 88 twin births, of which 36 were post-Gulf War, and no triplet or higher order births. The multiple birth ratio was 13.3/1000 livebirths. No statistical association between Gulf War deployment and twin/multiple births was detected, after adjustment for age differences (adjusted OR= 0.89, 95 percent CI 0.54, 1.48) (data not shown).

Total reproductive losses

A total of 1082 reproductive losses were reported, of which 484 occurred after the Gulf War. Gulf War deployment was not associated with an increased odds of reproductive losses overall (adjusted OR= 1.17, 95 percent CI 0.94, 1.45). Women with previous ectopic pregnancies or stillbirths had a higher odds of reproductive losses in 1991-1995 (Table 3).

Stillbirths

Fifty-five stillbirths were reported by survey participants overall, of which 23 occurred post-Gulf War. There was no statistically significant difference in the odds of stillbirths among

Gulf War veterans when compared to nondeployed veterans. (adjusted OR= 1.30, 95 percent CI 0.54, 3.13) (Table 3).

Ectopic pregnancies

One hundred twenty-nine ectopic pregnancies were reported, 74 of which occurred post-Gulf War. None resulted in a livebirth. No statistical association between ectopic pregnancy and Gulf War deployment was noted (adjusted OR= 1.51, 95 percent CI 0.90, 2.54) (Table 3). Not unexpectedly, previous ectopic pregnancies and stillbirths were strongly associated with ectopic pregnancies post-Gulf War (adjusted OR= 7.40, 95 percent CI 2.35, 23.27).

Miscarriages/spontaneous abortions

A total of 898 miscarriages were reported, of which 387 were post-Gulf War. The odds of miscarriages post-Gulf War was not significantly increased, after adjustment for the contributing effects of age, race/ethnicity, educational level, military component, and previous reproductive outcomes (adjusted OR= 1.25, 95 percent CI 0.99, 1.58) (Table 3).

Subfertility

A total of 1964 subjects provided information on the number of menstrual cycles before the last conception. The odds of Gulf War veterans reporting subfertility were no different than that for nondeployed veterans (adjusted OR= 1.11, 95 percent CI 0.85, 1.45). Subjects who reported previous ectopic pregnancies or stillbirths had a lower odds of reporting subfertility (adjusted OR= 0.42, 95 percent CI 0.22, 0.82) (Table 4).

Validation of self-reported outcomes

Table 5 presents the percentage of reported reproductive outcomes in which medical records was available to validate questionnaire responses. Generally, higher validation was observed with the more severe reproductive losses. Validation of reported miscarriages was low.

COMMENT AND CONCLUSIONS

Several previous studies have assessed the possibility of adverse reproductive outcomes in veterans of the 1991 Gulf War. Penman et al. ⁷ found no association of Gulf War deployment with ill health or birth defects in 2 units of the Mississippi National Guard. Internal Air Force ¹⁵ and Army ⁵, ⁶ investigations of pregnancy outcomes and miscarriages in Gulf War veterans also found no consistent pattern.

Other studies identified potential sources of concern. A postal survey of present and former Pennsylvania and Hawaii active-duty, Reserve, and National Guard service members 16, found that deployed reservists had a greater likelihood of reporting "menstrual difficulties" than nondeployed reservists. A study among Iowa military veterans found a higher prevalence of complaints of sexual discomfort among Gulf War veterans and their female partners 17.

With regard to birth defects, to date no increased general or specific risk related to Gulf War deployment has been definitively identified to date 8, 9.

We have found in a nationwide probability sample of 1991-era female veterans no results supporting the hypothesis of increased subfertility, reproductive losses, or LBW births among veterans of the Gulf War. In the absence of such results, the finding of a lower odds of births overall among Gulf War veterans may have been more a reflection of life choices made by service members and their spouses. Again, the absence of an association between Gulf War service and subfertility would indicate that there was no decrease in fertility associated with Gulf War service. Therefore, our data do not suggest that the lower odds of births overall in Gulf War veterans was despite attempts to conceive. In a companion article (Sato et al, Naval Health Research Center, unpublished manuscript) we noted that male Gulf War veterans and their wives reported an increased odds of miscarriages in the two years immediately following the Gulf War.

As discussed in that article, we believe that these results should be interpreted in the light of our concerns that differential response rates between Gulf War deployed and nondeployed veterans, where the nondeployed were underrepresented among the study respondents, may have influenced this finding. Study participation rates were also lower among male veterans, at 62 percent (Sato et al, Naval Health Research Center, unpublished manuscript) compared to approximately 72 percent for this study.

Another accompanying article (Araneta et al, Naval Health Research Center, unpublished manuscript), reports on a related study looking at pregnancy outcomes among female Gulf War veterans on active duty, who had pregnancy-related military hospitalizations on dates suggestive of a Gulf War exposed conception. In contrast to our study, Araneta et al found that postwar conceptions reported by subjects were at increased odds of resulting in miscarriage or ectopic pregnancy. Important methodological differences are likely to largely account for the differences in results. Araneta and her co-workers included any female veteran of any age group identified as having had a potentially Gulf War exposed conception based on military hospitalization data, married or unmarried. Also, there were differences in study participation rates, as well as sample selection effects resulting from looking at births in military hospitals alone, given that probably 40 percent or more of births in families of active duty personnel take place in non-military hospitals. (William Honner, Naval Health Research Center, personal communication, 1999).

Several limitations are inherent in the design of our own study. Our objective was to assess the post-Gulf War reproductive health of female Gulf War veterans when compared with nondeployed veterans. To this end, we adopted a postal self-reported survey format, enabling a sample population that was drawn from residents of all states and territories, as well as from all

of the services and components. Because of this choice of format, we did not collect data on potential Gulf War exposures and other reproductive risk factors. The addition of questions on exposure and risk factors would have considerably increased the length of the questionnaire, given the large number of putative exposures that have been suggested. Further, the viability of collecting valid risk factor and exposure data using a mailed, self-completed method has been questioned ¹⁸.

Although participation was high compared with other comparable mail surveys among military veterans ¹⁶, ¹⁹, it remains possible that nonresponse bias could have influenced the observed differences. Relatively small differences were observed in the demographic profiles between survey respondents and nonrespondents and adjusted accordingly in multivariate modeling.

We attempted to validate survey responses, using Department of Defense electronic data on hospitalizations in military medical treatment facilities. These data are available in a central database from fiscal year 1989 to date. We were unable to access data on hospitalizations by military personnel and their dependents in nonmilitary, civilian medical treatment facilities, nor to ambulatory care data in military medical treatment facilities for 1991-1995. Therefore, not unexpectedly, validation rates of self-reported outcomes were low. This low rate of validation leaves open the potential for recall and response bias influencing study results. We note though, that balanced survey response rates were obtained from nondeployed veterans and Gulf War veterans. Disproportionate response rates of either nondeployed veterans or and Gulf War veterans would have made the results more likely to be subject to a response or recall bias.

Finally, deployment to the Gulf War theater of operations was the measure of exposure.

This is a relatively insensitive index of exposure, given that the theater of operations

encompassed a very large geographic area ²⁰. We were unable to exclude exposure to some agent or agents within this broad definition that may have adversely affected specific groups of Gulf War veterans. However, no such groups have consistently been identified, either by investigations initiated among certain units where apparent clusters of complaints have occurred 16, 17, 20, 21, or observed in the large registries of cases maintained by the Department of Defense and the Department of Veterans Affairs ³, ²². Nonetheless, while a widespread pathologic process leading to increases in subfertility, reproductive losses, or LBW births among female Gulf War veterans was not found, additional studies will be required to confirm the absence of a pathologic basis to the reduction in the odds of births overall, and to exclude the possibility of multiple pathologic processes affecting the reproductive health of different clusters of Gulf War veterans.

ACKNOWLEDGMENTS

The authors thank Robert J. Reed (Naval Health Research Center, San Diego, CA) for assistance in data validation; and Tyler C. Smith (also of the Naval Health Research Center) for advising on the data analysis. We gratefully acknowledge the crucial contributions of Dr. Rebecca L. Calderon (Environmental Protection Agency, Research Triangle Park, NC) to the design of this study. We are also grateful to the Defense Manpower Data Center, Seaside, California, for its assistance in selecting the population sample.

REFERENCES

- 1. Briggs J, Miller K, Hudson D. The tiny victims of Desert Storm: has our country abandoned them? *Life Magazine*; 1995:45-61.
- Presidential Advisory Committee on Gulf War Veterans' Illnesses. Final report,
 December 1996. Washington, DC: US GPO; 1996.
- US Senate Committee on Veterans' Affairs. Report of the Special Investigation Unit on Gulf War Illnesses, One Hundred Fifth Congress, S. Prt. 105-39, Part I. Washington, DC: US GPO; 1998.
- Sylvester R, Chambers D. New theory on "Gulf War syndrome". Washington Times.
 Washington, DC; 1995:D8.
- Broadnax G. Abortion rates post-Desert Storm. Washington, DC: US Department of the Army, Office of the Surgeon General; 1992.
- 6. Rosa C. Spontaneous abortion rate and the Gulf War mobilization. *J US Army Medical Department* 1993;September-October 1993.
- 7. Penman AD, Tarver RS, Currier MM. No evidence of increase in birth defects and health problems among children born to Persian Gulf War veterans in Mississippi. *Mil Med*. 1996;161:1-6.
- 8. Araneta M, Moore CA, Olney RS, et al. Goldenhar syndrome among infants born in military hospitals to Gulf War veterans. *Teratology*. 1997;56:244-251.
- Cowan DN, DeFraites RF, Gray GC, Goldenbaum MB, Wishik SM. The risk of birth defects among children of Persian Gulf War veterans. N Engl J Med. 1997;336:1650-1656.

- US General Accounting Office. Operation Desert Storm: potential for reproductive dysfuction is not being adequately monitored. Washington, DC: US GAO; 1994.
- Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses.
 Annual report, November 1996 November 1997. Washington, DC: US Department of Defense; 1997.
- 12. Baird D, Wilcox, AJ, Weinburg, CR. Use of time to pregnancy to study environmental exposures. *Am J Epidemiol*. 1986;124:470-480.
- 13. Kline J, Stein Z, Susser M. Conception and reproductive loss: probabilities. In: Kline J, Stein Z, Susser M, eds. *Conception to birth. Epidemiology of prenatal development*. New York, NY: Oxford University Press; 1989;43-68.
- Institute of Medicine. Reproductive Effects. . Veterans and Agent Orange: update 1996.
 Washington, DC: National Academy of Sciences; 1996.
- Eggert R. Final report of Robins AFB, Georgia investigation. Brooks Air Force Base,
 TX: US Department of the Air Force; 1994.
- 16. Stretch RH, Bliese PD, Marlowe DH, Wright KM, Knudson KH, Hoover CH. Physical health symptomatology of Gulf War-era service personnel from the states of Pennsylvania and Hawaii. *Mil Med.* 1995;160:131-136.
- Iowa Persian Gulf War Study Group. Self-reported illness and health status among Gulf
 War veterans. A population-based study. JAMA. 1997;277:238-245.
- McCauley L, Joos, SK, Spencer, PS, Lasarev, M, Shuell, T. Strategies to assess validity of self-reported exposures during the Persian Gulf War. *Environ Res.* 1999;81:195-205.

- 19. Araneta MRG, Kamens DR, Gastanaga, VM, et al. Reproductive and perinatal outcomes among conceptions and pregnancies during the Persian Gulf War. Conference on Federally Sponsored Gulf War Veterans Illnesses Research. Arlington, VA; 1998.
- 20. Gray GC, Kaiser KS, Hawksworth AW, Hall FW, Barrett-Connor E. Increased postwar symptoms of psychological morbidity among US Navy Gulf War veterans. *Am J Trop Med Hyg.* 1999; 60(5)758-766.
- 21. Fukuda K, Nisenbaum R, Stewart G, et al. Chronic multisymptom illness affecting Air Force veterans of the Gulf War. *JAMA*. 1998;280:981-988.
- Presidential Advisory Committee on Gulf War Veterans' Illnesses. Special report,
 November 1997. Washington, DC: US GPO; 1997.

FIGURE 1. Birth outcomes reported by female service members, 1991-1995, by birth weight.

Footnote: * National vital statistics on births for 1995 from the National Center for Health

Statistics (NCHS), presented for comparison purpose

TABLE 1. Demographic data

	Sample		
	Population	Responders	p value
	N = 8251	N = 4435	
	%	%	
Deployment status	· · · · · · · · · · · · · · · · · · ·	f	NS
Nondeployed	50.20	50.60	
Gulf War deployed	49.80	49.40	•
Age group, in years			< 0.001
≤19	6.42	5.85	
20-24	38.09	34.65	
25-29	34.77	36.35	
≥30	20.72	23.15	
Race/ethnicity			<0.001
White	60.13	67.00	
Black	31.24	25.10	
Hispanic	4.39	4.10	
Other	4.24	3.90	
Highest educational level			< 0.001
High school or less	73.22	68.61	
College	10.18	13.26	
Postgraduate	1.72	2.12	
No information	14.88	16.01	
Service			< 0.001

Army	49.86	45.40	
Navy	18.81	20.00	
Air Force	26.88	29.80	
Marine Corps	4.45	4.80	
Service component	:		< 0.001
Active duty	85.35	86.70	
Reserve	10.80	9.40	
National Guard	3.85	3.90	

NS = Not significant.

TABLE 1. Demographic data (cont)

TABLE 2. Singleton birth outcomes, by Gulf War deployment status, military, and demographic covariates

	Mac	Macrosomic	Normal	Normal weight births	LBW	LBW* births	All	All births
-	births ((≥4000 g)	(2500	(2500-3999 g)	3	(<2500 g)		
•	Ž	N=323	Ż	N=2238	Ż	N=152	Ż	N=2713
	AOR†	95% CI‡	AOR	95% CI	AOR	95% CI	AOR	95% CI
Deployment Status								
Nondeployed §								
Gulf War deployment	0.86	0.66, 1.12	0.87	0.71, 1.07	0.93	0.63, 1.38	0.58	0.44, 0.77
Age group, in years				:				
< 19 §								
20-24	0.99	0.60, 1.62	96.0	0.64, 1.46	1.82	0.71, 4.69	1.40	0.81, 2.42
25-29	1.02	0.61, 1.71	0.81	0.53, 1.24	1.79	0.68, 4.72	0.97	0.56, 1.69
≥30	0.83	0.46, 1.52	0.84	0.52, 1.35	2.20	0.77, 6.31	0.88	0.48, 1.63
Race/ethnicity								
White §			•					
Black	0.45	0.30, 0.65	0.78	0.62, 0.99	2.09	1.37, 3.16	0.59	0.44, 0.80
Hispanic	0.85	0.51, 1.44	0.89	0.59, 1.32	99.0	0.23, 1.85	0.71	0.43, 1.19

								47
Other	-89.0	0.36, 1.30	1.89	1.08, 3.32	0.62	0.19, 2.03	2.43	0.97, 6.11
Highest educational level	ī					,		
High school or less §								
College	0.71	0.50, 1.00	1.10	0.83, 1.46	1.39	0.73, 2.66	0.83	0.55, 1.26
Postgraduate	1.05	0.60, 1.82	1.21	0.74, 1.97	1.24	0.45, 3.42	1.03	0.51, 2.08
Service component								
Active duty §								
Reserve	0.75	0.38, 1.48	1.13	0.70, 1.83	0.53	0.16, 1.74	0.93	0.52, 1.65
National Guard	0.30	0.07, 1.30	1.18	0.58, 2.42	1.27	0.37, 4.38	0.83	0.37, 1.89
Pre-1991 outcomes								
None	0.91	0.53, 1.54	2.38	1.62, 3.50	0.82	0.36, 1.88	2.74	1.70, 4.43
LBW births	0.16	0.02, 1.23	1.39	0.71, 2.70	1.44	0.47, 4.47	1.23	0.56, 2.70
Macrosomic births	2.79	1.63, 4.77	0.70	0.45, 1.09	0.14	0.02, 1.10	1.25	0.69, 2.28
Normal weight births	0.62	0.37, 1.03	2.52	1.74, 3.64	0.43	0.19, 1.01	2.58	1.62, 4.10
Miscarriages	0.89	0.51, 1.55	1.54	1.03, 2.31	0.42	0.15, 1.19	1.37	0.82, 2.27
Ectopics and stillbirths	F	T	0.55	0.25, 1.20	2.30	0.66, 8.06	0.36	0.16, 0.82

* LBW: Low birth weight; † AOR: Adjusted odds ratio; ‡ CI: Confidence interval; § Reference category; ¶ Insufficient data.

TABLE 2. Singleton birth outcomes, by Gulf War deployment status, military, and demographic covariates (cont)

TABLE 3. Stillbirths, ectopic pregnancies, miscarriages, and total reproductive losses

	[i3S	Stillbirths	Ectopic	Ectopic pregnancies	Misc	Miscarriages	Total repro	Total reproductive losses
· .	Z	N=23	Z	N=74	Ż	N=387	Z	N=484
14	AOR*	95% CI†	AOR	95% CI	AOR	95% CI	AOR	95% CI
Deployment Status								
Nondeployed‡								
Gulf War deployed	1.30	0.54, 3.13	1.51	0.90, 2.54	1.25	0.99, 1.58	1.17	0.94, 1.45
Age group, in years							·	
< 25 ‡								
25-29	1.96	0.72, 5.37	1.71	0.98, 3.00	0.99	0.77, 1.27	1.10	0.87, 1.40
> 30	2.31	0.64, 8.36	2.17	1.07, 4.38	1.03	0.73, 1.44	1.25	0.91, 1.71
Race/ethnicity								
White ‡								
Black	4.88	1.88, 12.66	2.50	1.47, 4.28	1.08	0.82, 1.42	1.30	1.01, 1.67
Hispanic, other	0.77	0.09, 6.32	1.34	0.58, 3.11	98.0	0.59, 1.26	0.85	0.60, 1.22
Highest educational level								
High school or less ‡								
College or higher	1.27	0.28, 5.68	98.0	041, 1.80	1.32	0.93, 1.86	1.26	0.91, 1.73

Service component

1.68 1.08, 2.62	0.96 0.45, 2.05		0.72 0.48, 1.10	0.76 0.37, 1.57	0.94 0.56, 1.57	0.59 0.40, 0.88	1.30 0.87, 1.96	3.88 1.76, 8.55
1.09, 2.76	0.30, 1.77		0.46, 1.12	0.15, 1.03	0.63, 1.83	0.44, 1.02	0.85, 2.00	1.10, 5.62
1.73	0.73		0.72	0.39	1.08	19.0	1.30	2.48
0.34, 2.98	0.73, 7.28		0.42, 2.90	0.50, 6.27	0.10, 2.18	0.16, 1.05	0.85, 5.06	2.35, 23.27
1.01	2.31		1.11	1.77	0.47	0.42	2.07	7.40
« ОЭ	∞	S	0.10, 3.30	0.31, 14.30	ø	0.10, 3.06	∞,	0.19-21.33
Ø	w		0.58	2.09	∞	0.56	60 0	1.99
	National Guard	Pre-1991 outcomes		LBW¶ births	Macrosomic births	Normal weight births	Miscarriages	Ectopics and stillbirths

^{*} AOR: Adjusted odds ratio; † CI: Confidence interval; ‡ Reference category; § Insufficient data; ¶ LBW: Low birth weight.

TABLE 3. Stillbirths, ectopic pregnancies, miscarriages, and total reproductive losses (cont)

TABLE 4. Reported subfertility, by Gulf War status and military/demographic covariates

· · · · · · · · · · · · · · · · · · ·	Su	bfertility
	N	I=1964
	AOR*	95% CI†
Deployment status	i	
Nondeployed ‡		
Gulf War deployed	1.11	0.85, 1.45
Age group, in years		
< 25 ‡		
25-29	1.06	0.85, 1.45
≥ 30	0.73	0.52, 1.02
Race/ethnicity		
White ‡		
Black	1.40	1.01, 1.95
Hispanic, other	1.86	0.98, 3.56
Highest educational level		
High school or less ‡		
College	0.87	0.59, 1.29
Postgraduate	1.06	0.57, 1.96
Service component		
Active duty ‡		
Reserve	1.05	0.60, 1.83
National Guard	0.93	0.34, 2.49

Previous outcomes	•	
None	1.02	0.57, 1.81
LBW ¶ births	0.86	0.52, 1.42
Macrosomic births	1.42	0.94, 2.16
Normal weight births	1.45	1.03, 2.04
Miscarriages	0.89	0.65, 1.22
Ectopics and stillbirths	0.42	0.22, 0.82

^{*} AOR: Adjusted odds ratio; † CI: Confidence interval; ‡ Reference category;

TABLE 4. Reported subfertility, by Gulf War status and military/demographic covariates (cont)

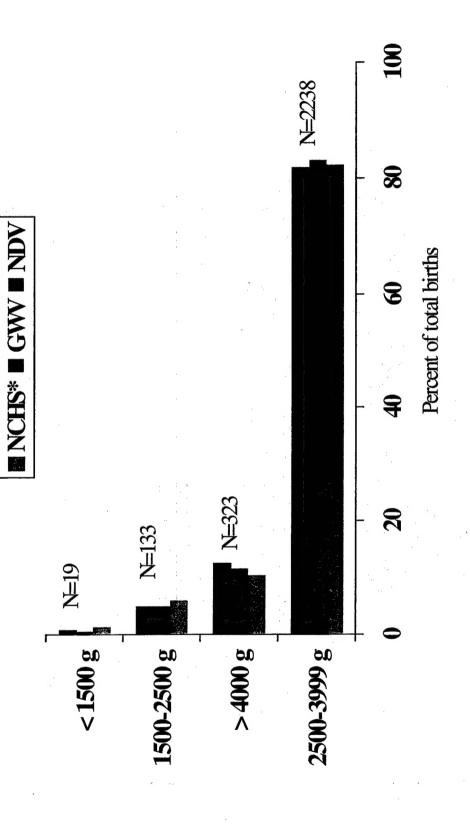
[¶] LBW: Low birth weight.

TABLE 5. Validation against hospitalization data of reproductive losses reported by female service members, by Gulf War deployment status

	G	ulf War vetera	ns	Nor	ideployed vete	erans
	Reported *	Validated †	% Validated	Reported	Validated	% Validated
Miscarriages	263	62	23.6	301	95	31.6
Stillbirths	14	5	35.7	14	7	50.0
Ectopic	42	16	38.1	46	26	56.5
pregnancies						

^{*} Reproductive losses self-reported in survey by subjects.

[†] Discharge diagnosis ICD-9 code consistent with reported reproductive loss recorded in database for military medical treatment facility hospitalizations for year of self-reported outcome.



REPORT DOCUMENTATION PAGE

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB Control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

1. Report Date (DD MM YY) 08/23/00	2. Report Type New	3. DATES COVERED (from - to) Jan 1996 to Feb 2000
4. TITLE AND SUBTITLE Reproductive Outcomes am No Evidence of Increased M	ong Female Gulf War-era US Military Veterans: lorbidity	5a. Contract Number: 5b. Grant Number: 5c. Program Element: 5d. Project Number:
Christy M. Anderson, B.A.; Debor	M. Hiliopoulos, M.P.H., M.B.A.; Linda Wang, B.S.; ah R. Kamens, M.B.A.; Jacqueline M. Major, M.S.; P. Poblete, B.A.; Andrew C. Zau, M.P.H.; Gregory C. Gray,	5e. Task Number: 5f. Work Unit Number: 60002 5g. CPHS Approval Number: 30276
7. PERFORMING ORGANIZATION Naval Health Research C P.O. Box 85122 San Diego, CA 92186-512	enter	9. PERFORMING ORGANIZATION REPORT
8. SPONSORING/MONITORING A Chief, Bureau of Medicine MED-02	AGENCY NAMES(S) AND ADDRESS(ES) and Surgery	Report No. 00-38
2300 E St NW Washington DC 20372-530	00	10. Sponsor/Monitor's Acronyms(s) BUMED 11. Sponsor/Monitor's Report Number(s)

12 DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Veterans of the Persian Gulf War have complained of III health, with diverse symptoms, since the war's end. We report here on postwar reproductive outcomes among female Gulf War veterans, compared with those in 1991-era nondeployed veterans. Since 1996, a stratified, probability-based sample of 8,251 deployed and nondeployed female military veterans, aged 18-33 years and married, has been mailed a reproductive health survey. A total of 2,349 Gulf War Veterans and 2,507 nondeployed veterans returned the questionnaires, for a participation rate of 71.7 percent. Adjusted for age, race/ethnicity, educational attainment, military component, and pre-1991 reproductive outcomes, no statistically significant differences between female Gulf War veterans and nondeployed veterans were identified in the odds of reporting a live, normal, full-term, macrosomic (birth weight ≥ 4,000 g) or a low birth weight (< 2,500 g) birth, or among stillbirths, ectopic pregnancies, miscarriages, and subfertility. No differences were noted among twin or higher multiple births. Although symptoms of reproductive III health have been reported by veterans of the 1991 Gulf War, this large-scale and broad-based survey of the reproductive health of 1991-era US military veterans survey suggests that the reproductive health of female Gulf War veterans was unaffected by their deployment to the Gulf War.

15. SUBJECT TERMS

Gulf War, female veterans, reproductive outcomes, subfertility

16. SECURIT	Y CLASSIFICAT			18. NUMBER	19a. NAME OF RESPONSIBLE PERSON
a. REPORT UNCL	b.ABSTRACT UNCL	c. THIS PAGE UNCL	OF ABSTRACT UNCL	30	Commanding Officer 19b. TELEPHONE NUMBER (INCLUDING AREA CODE)
				50	COMM/DSN: (619) 553-8429